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LETTER TO EDITOR

Development Of Post Tubercular , Bronchial Asthma –A Pilot Study

SHETTY A J , TYAGI A

ABSTRACT

Pulmonary impairment associated with obstructive airway disease is recognized as a common complication of advanced tuberculosis. Most patients suffering from tuberculosis with moderate to far advanced post treatment residual lung lesions exhibit symptoms of impaired pulmonary functions due to persistent airway obstruction but why do only a small proportion develop reversible airway obstruction to qualify for post tuberculosis bronchial asthma categorization? The present study was aimed to investigate if antitubercular drugs were involved in the pathophysiology of post-tubercular bronchial asthma. Asthmatic patients with past history of pulmonary tuberculosis who visited the hospital for treatment between Jan - Dec 2006 and 16 patients who had history of pulmonary tuberculosis and had successfully completed anti tubercular therapy but did not develop asthma were randomly chosen. During the study period there were 20 asthmatic patients with past history of antitubercular drug therapy. *With 6 months* of antitubercular therapy, 6 out of 20 pulmonary tuberculosis patients developed asthma (40%) and 9 out of 16 patients took 6 months of antituberculars but did not develop asthma (60%). p= 0.3, found not significant. *With 8 months* of antitubercular therapy, 14 out of 20 patients developed asthma (66.7%) and 7 out of 16 patients did not develop asthma (33.3%) . p= 0.5, found not significant. (Fishers test).

Conclusion : Anti tubercular drugs do not appear to play a role in the development of post tubercular bronchial asthma.

Key Words : antitubercular drugs, posttuberculosis bronchial asthma.

Corresponding Author:
Dr. Shetty Akhila .J.
Associate Professor
Department Of Pharmacology
Kasturba Medical College, Manipal University
Light House Hill Road
Mangalore 575001
Email - shettyakhila@yahoo.com

Introduction

Tuberculosis is a global emergency needing aggressive control measures. Similarly bronchial asthma is a major global health problem affecting people of all ages. However, both these health problems do not reach peak of activity simultaneously due to different immunological mechanisms requiring Th 1 and Th 2 lymphocytes for mediating tuberculosis and asthma respectively. A proportion of pulmonary tuberculosis patients later develop asthma, after the enhanced Th 1 lymphocytes have been reduced to the normal level with anti-tuberculosis treatment [1]. Co-occurrence of asthma and active tuberculosis is uncommon. Airway obstruction is one of the known complication / sequeal of tuberculosis [1], which on aggravation emerges as bronchial asthma.

Pulmonary impairment associated with obstructive airways disease is recognized as a common complication of advanced tuberculosis. Most tuberculosis patients with moderate to far advanced post-treatment residual lung lesions exhibit symptoms of impaired pulmonary functions due to persistent airways obstruction, but only a small proportion develop reversible airways obstruction to qualify for post- tuberculosis bronchial asthma categorization. Could the development of post tubercular bronchial asthma be related to antitubercular drugs?

The standard drugs used in treatment of tuberculosis are Isonicotinic acid hydrazide (H), Rifampicin (R), Streptomycin (S)and Pyrazinamide (Z), these drugs are bactericidal. The bacteriostatic drugs are Ethambutol (E)and Thiacetazone. The Reserve drugs are Capreomycin, Kanamycin, Amikacin and Fluoroquinolones which are bactericidal and Ethionamide, Cycloserine and clofazimine which are bacteriostatic [2].

But there are no reports on their toxicity on pulmonary system.

Materials And Methods

The study was conducted after approval from the institutional ethics committee. Data was collected and analysed in KMC Hospital Attavara after approval from the DMO / RMO and COO respectively.
Inclusion criteria:

1. Asthmatic patients as diagnosted by physicians using standard guidlings with past history of pulmonary tuberculosis belonging to category I / II and who had visited the hospitals for treatment between Jan - Dec 2006 (n=20).

2. Patients who had history of pulmonary tuberculosis, belonging to category I / II and had successfully completed anti tubercular therapy but did not develop asthma (n=16 randomly chosen).

Exclusion Criteria

Patients with irregular antitubercular treatment history.The hospital records of the patients who had bronchial asthma were analyzed retrospectively to check their anti-tubercular treatment history and 16 patients with past history of pulmonary tuberculosis and completed therapy and were sputum negative with no X Ray lung impairment and with no signs and symptoms suggestive of bronchial asthma were randomly choosen to serve as controls.

Results

20 patients of ages between 35 –years developed post tubercular asthma between Jan-Dec 2006, male: female = 12 : 8 and 2 males were smokers ; 5 had family history of Asthma/allergy (25%). 19 patients (73%) had the first episode of asthma after stopping chemotherapy within 3 yrs. Among the 16 patients who did not develop bronchial asthma, male: female = 10: 6 and 3 males were smokers; 3 had family history of bronchial asthma (19%),. They were of ages between 38 –years [Table/Fig 1].

(Table/Fig 1) Number Of Patients Who Did And Did Not Develop Asthma With Category I And Category II Anti Tubercular Drugs

DOTS Category:	Patients who developed Bronchial Asthma (20)	Patients who did not developed Bronchial Asthma (16)
Category I*	6 (40%)	9 (60%)
Category II**	14 (66.7%)	7 (33.3%)

*** Category I - 6 months of Anti-Tubercular treatment with HRZE**
**** Category II - 8 months of Anti-Tubercular treatment with HRZES**

Fisher's test was applied for statistical analysis. Level of significance was set at <0.05.

With 6 months of therapy, 6 out of 20 patients developed asthma (40%). 9 out of 16 patients took antituberculars for 6 months but did not develop asthma (60%). p= 0.3, found **not** significant. With 8 months of therapy, 14 out of 20 patients developed asthma (66.7%) . 7 out of 16 patients who took antituberculars did not develop asthma (33.3%) . p= 0.5, found **not** significant [Table/Fig 2].

(Table/Fig 2) Smoking And Development Of Post Tubercular Bronchial Asthma.

Patients who developed Bronchial Asthma		Patients who did not develop Bronchial Asthma	
20		16	
Males	12	Males	10
Non-Smokers	10	Non- Smokers	7
Smokers	2	Smokers	3

Discussion

For the year 2000 the burden of TB was 8.5 million [3]. India accounts for nearly 30% of global tuberculosis burden annually [4]. Post tuberculosis bronchial asthma is a separate clinical entity. The present study

was conducted to observe if the development of post tubercular bronchial asthma was related to the anti tubercular drugs used by the pulmonary tuberculosis patients.

The mechanism of evolution of post-tuberculosis bronchial asthma is related to the immunopathogenesis of tuberculosis and bronchial asthma [5]. The Th 1 and Th 2 sub-groups of T lymphocytes regulate development of tuberculosis and bronchial asthma and their levels are not enhanced simultaneously [5]. The Th 1 lymphocytes preferentially produce and secrete IL-2 which stimulates T lymphocyte proliferation and Interferon –gamma formation. IFN-gamma in turn inhibits B cell activation and the resultant IgE synthesis. Thus IL-2 triggered pathway is responsible for the type IV hypersensitivity reaction [5],[6],[7]. The Th 2 lymphocytes, produce and secrete IL-3, IL-4, IL-5, IL-9 and IL-13; the specific actions of these interleukins produce the characteristic inflammatory response of asthma [5],[6],[7].

The anti tubercular drugs do not seem to modulate the cell mediated immunity since the results of the study indicate that antitubercular drugs do not play a role in development of post tubercular bronchial asthma. The pathogenesis of development of post-tubercular bronchial asthma could be due to the retained cell mediated immunity to the possible presence of a few inactive M. tuberculi even after treatment.

Limitation of this study was its small numbers. It is hoped that following this larger data will be studied in the future.

Conclusion

Anti tubercular agents does not appear to play a role in the development of post tubercular bronchial asthma based on this pilot study but a larger data needs to be evaluated to answer this question.

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